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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LUNDGREN, JEFFREY S	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 11/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/726,624	LI, MIN	
	Examiner	Art Unit	
	Jeff Lundgren	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54,57,66 and 69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54,57,66 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *see office action*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Reassignment of Application

Please note that this application has been reassigned to Examiner Jeffrey Lundgren. In order to expedite accurate processing of the application papers, all future correspondence with the Office should reflect this change.

Status of the Claims

In the previous Office Action mailed on December 29, 2005, the Examiner indicated that claims 54, 57, 66 and 69 would be considered allowable if rewritten in independent form.

However, allowability of these claims is withdrawn for the reasons presented in the Office Action below.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on November 30, 2000, has been considered by the Examiner. The submission is in compliance with the provisions of 37 CFR § 1.97. Enclosed with this Office Action is a return-copy of the Form PTO-1449 with the Examiner's initials and signature indicating those references that have been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 54, 57, 66 and 69, are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 54, 57, 66 and 69, are indefinite for reciting the phrase "specifically bind(s)" because one of ordinary skill in the art would not reasonably be able to determine the metes and bounds of the claim. The phrase is a relative phrase and it is not clear if this is a quantitative or

qualitative phrase[1]; the phrase is neither art accepted (i.e., does not have an adequately art-accepted definition), nor is the phrase reasonably defined in the specification. For example, the specification states the following:

> "A ligand can be previously determined to ***specifically bind*** the selected protein by any known, standard means for determining such binding or, for example, as described herein. A ligand can include, for example, a peptide hormone, a toxin, a fragment from a large protein."

Specification, page 8, second paragraph (emphasis added). Applicants may overcome this rejection by deleting the term "specifically."

Claims 54, 57, 66 and 69, are indefinite for reciting the phrase "wherein the ligand has been previously demonstrated to ...bind to the cellular protein," because one of ordinary skill in the art may or may not be aware of previous binding determinations. The limitation is expressed in the claim as an inherent property of the ligand, however, it is not a property of the ligand. Applicants may overcome this rejection by deleting this phrase. Applicants may rewrite this limitation as a positive proactive step of the claim (*e.g.*, "determining the binding of a ligand to a selected cellular protein," followed by "expressing the ligand on the surface of a recombinant virus, contacting the cell with a population of the recombinant virus expressing the ligand on the surface...").

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 54 and 66 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Goodson *et al.*, *Proc. Natl. Acad. Sci. 91*:7129-7133 (**1994**), in view of Zhou *et al.*, *Journal of*

[1] For example, binding is a property that is often quantified by a binding constant or a dissociation constant. However, in comparing monoclonal antibodies to polyclonal antibodies, there are different avidities and affinities, but it is not clear whether or not either or both binders would meet Applicants' definition of a "specific binding" event.

Neurochemistry 66(2):620-628 (**1996**), as evidenced by Bigge *et al.*, U.S. Patent No. 5,489,717, issued on February 6, 1996.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 54 and 66 are directed to detecting the presence of a selected cellular protein on the surface of a cell by binding a virus/bacteriophage expressing a ligand, wherein the ligand binds to the protein, wherein the cell surface protein is NMDA.

Goodson teaches a method for the affinity selection of randomly generated 15-mer peptides displayed on bacteriophage M13 (*i.e.*, bacteriophage/virus) to identify ligands of the urokinase receptor. After initial identification of certain phage that bind the target receptor, the selected phage were tested in a competitive binding assay with a receptor-binding compound. Goodson teaches the binding of the phage candidates with the cell-bound receptor:

> "A peptide derived from the EGF-like domain of human urokinase, residues 12-32, with Cys-19 converted to Ala, competes with ATF for binding to uPAR with an IC50 of 100nM (30). To verify that bacteriophage displaying a uPAR ligand could be specifically selected by cell-surface uPAR, we constructed a positive control bacteriophage, encoding uPA 13-32C19A. ***As shown in Table 1, both COS-7 and baculovirus-infected Sf9 cells displaying human uPAR selectively enriched for the uPA 13-32C19A bacteriophage over a control bacteriophage by 500- and 800-fold, respectively.*** In addition, control cells expressing the substance P receptor did not enrich for this uPA bacteriophage. ***The random peptide bacteriophage display library, consisting of 107 different 15-mers, was then affinity selected for three rounds alternately on Sf9 cells and COS-7 cells expressing uPAR.*** Enrichment for uPAR ligands was initially assessed by bacteriophage yield. After two rounds of selection the yield had increased 30-fold over the first round, and the third round showed a further increase of 130-fold to 5.4%, approximately that seen for the positive control bacteriophage. The overall yield increase was 4000-fold.

> Individual plaques were picked from the third round eluate and subjected to DNA sequence analysis. ***From 66 plaques, 19 different DNA and peptide sequences were obtained, and these individual bacteriophage were tested for binding to cells displaying uPAR***. Each of them showed 20- to 500-fold greater yields than an irrelevant bacteriophage. Peptides corresponding to the selected sequences were synthesized, purified, and tested as competitors in a uPAR binding assay with iodinated ATF as ligand (27). These results are summarized in Table 2, in comparison with known uPAR ligands."

Goodson, page 7131, col. 1, paragraphs 2 and 3 in the section having the heading, *Results* (emphasis added).

Although Goodson teaches the advantages and benefits of identifying peptide binding agents to the urokinase receptor as a means understanding certain aspects of the pathologies related to cancer and providing therapeutic options, Goodson does not explicitly relate his method of affinity maturation using bacteriophage applied to NMDA receptors and the corresponding pathologies:

> "We report here the identification and characterization of peptide antagonists with nanomolar affinity for the human uPAR by using a 15-mer peptide library. This extension of bacteriophage peptide display to cell-surface expressed proteins ***expands the utility of the method to a wide variety of biologically interesting targets***."

Goodson, page 7129, col. 2, first full-length paragraph (emphasis added).

Zhou teaches an investigation of certain peptide analogs of Conatokin-G that bind to NMDA receptors. Zhou teaches that certain of the analogs show improved NMDA receptor antagonism (page 626-627).

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed based on the teachings of Goodson and Zhou (as evidence by Begge), because each of Goodson and Zhou are directed to the development and testing of novel peptide analogs that act as cell surface protein antagonists. One would have been motivated to extend the methodology of Goodson to the NMDA receptor, because Zhou, as evidenced by Bigge, shows the improved binding properties that peptide analogs can provide as NMDA antagonists. Although not explicitly stated in Zhou, those of skill in would recognize the therapeutic utility of peptide NMDA antagonists, as disclosed by Bigge, for treating a number of

pathologies, such as Alzheimer's disease, and the usefulness in developing and characterizing new peptide analogs for binding NMDA receptors by the method of Goodson. Therefore, the invention as a whole was *prima facie* obvious at the time it was invented.

Conclusions

No claim is allowable.

If Applicants should amendment the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipsis verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSL

10/30/06
MY-CHAU T. TRAN
PATENT EXAMINER